at page 35, lines 1-4 of the specification, which teaches that beads may be distinguished and separated by physical-chemical characteristics, including size.

Claims 70-75 have been added. Support for the element that "the beads of each type are encoded with a physical characteristic that uniquely identifies the biomolecules attached to said bead type" as recited by claim 70 is found at page 35, lines 1-4 of the specification, which teaches that beads may be distinguished and separated by physical-chemical characteristics, including size.

Support for claim 71, which recites, *inter alia*, that the "planar array of beads is permanently anchored to a substrate," is found at page 16, lines 31-32, which states that "[a]n additional fundamental operation that complements the previous set is that of permanently anchoring an array to the substrate."

Support for claim 72, which recites, *inter alia*, that the "array of beads is anchored by chemical means", is found from page 16, line 31 to page 17, line 1, which states that permanently anchoring the array to the substrate "is best accomplished by invoking anchoring chemistries analogous to those relying on heterobifunctional cross-linking agents invoked to anchor proteins via amide bond formation."

Support for claim 73, which recites, *inter alia*, that the "array of beads is permanently anchored to said electrode", is found at page 19, lines 1-4, which states that "[t]hese arrays may be placed and delineated in designated areas of the substrate, and the interparticle spacing and internal state of order within the array may be controlled by adjusting the applied field prior to anchoring the array to the substrate."

Support for claims 74 and 75, which recite that "the beads of each type are encoded with a physical characteristic that uniquely identifies the biomolecules attached to said bead type"

(claim 74) and that "each of said beads are encoded with a chemical label that uniquely identifies the biomolecules attached to said bead type" (claim 75) is found at page 28, lines 25-30, which states

> To create the panel, a multi-component mixture of beads carrying, for example, compounds produced by bead-based combinatorial chemistry, is placed between the electrodes. Each type of bead may be present in multiple copies. Arrays are formed in response to an external field in a designated area of the electrode surface. This novel approach of in-situ assembly of panels relies on beads that carry a unique chemical label, or code, to permit their identification subsequent to the completion of a binding assay.

Additional support is provided on page 35, lines 2-4, which teaches that beads may be distinguished and separated on the basis of a physical property, such as size.

Applicants respectfully submit that no new matter has been added by the addition of new claims 70-75.

The specification and the drawings were also amended to cross-reference the related applications, and to ensure that the figure legends for Fig. 9 and Fig. 3 are consistent with the referenced drawings. A separate page containing a marked-up version of the amended paragraph of page 10 is also enclosed.

Applicant respectfully maintains that no new matter has been introduced by virtue of the amendments and requests their entry. Claims 43-53, 56, and 70-75 are now pending and under examination. In view of the amendments made herein and the remarks below, Applicant respectfully requests reconsideration and withdrawal of the rejections and objections set forth in the October 11, 2002 Office Action.

REJECTIONS UNDER 35 U.S.C. § 112

Claims 43 to 56 were rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite. The Examiner requested clarification as to whether the bead types are distinguished by biomolecules or by a unique chemical/physical characteristic.

Claims 54 and 55 were further rejected under 35 U.S.C. §112, second paragraph, as being allegedly indefinite, because the claims, although directed to a composition, recite a method step.

Claim 43 has been amended to present the claimed subject matter in a better form, without changing the scope of the invention. The amended claim is directed to a planar array of beads in a spatially non-random configuration. The array comprises a plurality of different bead types, wherein each of said bead types has a different biomolecule attached thereto capable of forming a complex with an analyte. The bead types are encoded with a chemical or physical characteristic that uniquely identifies the biomolecule of the bead type, and the array of beads is configured such that when the array of beads is contacted with liquid comprising an analyte, the beads of said array are in a continuous liquid phase. Applicant respectfully submits that the claim 43, as amended, overcomes the indefiniteness rejections set forth in the October 11, 2002 Office Action.

As to claims 54 and 55, these claims have been canceled, without acquiescing to the correctness of the Examiner's position, but merely to expedite the prosecution of the application.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

REJECTIONS UNDER 35 U.S.C. §102

Claims 43-47, 50-53 and 56 are rejected under 35 U.S.C. §102(e) as being allegedly anticipated by Chandler et al. (WO 99/19515). Claims 43, 47, 49-56 are rejected as being allegedly anticipated by Walt (WO99/18434). Applicant respectfully traverses the rejections.

As reflected in the application data sheet filed with the application on October 17, 2000, this application is a continuation of U.S. Patent No. 09/171,550, filed October 26, 1998, which in turn claims benefit of earlier filed applications, with the earliest filing date being that of U.S. Provisional Application Serial No. 60/016,642, filed on April 25, 1996.

Support for claims 43-53 and 56 is found throughout U.S. Provisional Application No. 60/016,642. For example, support for the claim element "a planar array of beads in a spatially non-random configuration" as recited in claim 43 is found at page 10, lines 1-5, which inherently teaches "beads in a spatially non-random configuration" by disclosing that arrays of colloidal particles may be placed in designated areas on the electrode surface. Further support for this element is provided by page 13, lines 5-9, which teaches that the internal state of order of a bead array is determined by the strength of the applied voltage, with higher values favoring increasingly denser packing of beads and the eventual formation of order arrays displaying a hexagonally crystalline configuration in the form of a bubble raft. Moreover, support for "beads in a spatially non-random configuration" is provided by Figures 2c, 2d, and 4b, which illustrate ordered arrays of beads on a surface.

Support for the claim element "a plurality of beads comprising different bead types, wherein each of said bead types has a different biomolecule attached thereto capable of forming a complex with an analyte" as recited in claim 43 is found at page 27, lines 16-23, which teaches that the present invention provides a method to produce a heterogeneous panel of beads and

potentially of biomolecules for presentation to analytes in an adjacent liquid. This part of the specification further teaches that a heterogeneous panel contains particles or biomolecules which differ in the nature of the chemical or biochemical binding sites that they offer to analytes in the solution.

The claim element "said beads are encoded with a chemical or physical characteristic that uniquely identifies the biomolecule of said bead type" as recited in claim 43 finds support at page 27, line 22 which teaches that "[t]he present method relies on the functional elements of the invention to assemble a planar array of a multi-component mixture of beads which carry chemical labels in the form of tag molecules and may be so identified subsequent to performing the assay." Further support is provided by page 36, lines 8 – 16, which teaches that beads may be distinguished and separated on the basis of size.

The claim element "said array of beads is configured such that when said array of beads is contacted with liquid comprising an analyte, the beads of said array are in a continuous liquid phase" as recited in claim 43 finds support at page 27, lines 17-19, which teaches

> The present invention provides a method to produce a heterogeneous panel of beads and potentially of biomolecules for presentation to analytes in an adjacent liquid. A heterogeneous panel contains particles or biomolecules which differ in the nature of the chemical or biochemical binding sites they offer to analytes in solution.

Additional support is found at page 29, lines 9-11, which states "[i]n contrast to all prior art methods, the present invention provides a novel method to create heterogeneous panels by in-situ, reversible formation of a planar array of "encoded" beads in solution adjacent to an electrode."

To summarize, U.S. Provisional Application No. 60/016,642 provides support for each and every claim of Applicant's independent claim 43.

Moreover, U.S. Provisional Application No. 60/016,642 also provides support for the pending dependent claims.

For example, support for claim 44, which recites, *inter alia*, that "the biomolecules comprise peptides and proteins" is found at page 44, lines 4-6, which states that "[t]he present invention can be used to implement solid phase hybridization assays in a planar format in a configuration related to that of a protein binding assay in which target molecules are chemically attached to colloidal beads." Additional support is found at page 41, lines 9-13, which discusses combinatorial synthesis of peptides in the context of bead based compound libraries of this invention.

Support for claim 45, which recites, *inter alia*, that "the biomolecules comprise oligonucleotides or nucleic acids" is found at page 44, lines 6-8, which states "[t]he methods of the present invention facilitate the formation of a planar array of different target oligonucleotides for presentation to a mixture of strands in solution." Additional support is found at page 44, line 11 to page 45, line 17, which discusses DNA analysis in the context of this invention.

Support for claim 46, which recites, *inter alia*, that "the biomolecules are selected from the group consisting of ligands, receptors, antigens, and antibodies" is found at page 29, lines 1-2 (ligands), page 33 lines 24-30 (receptors and antigens), and page 43 lines 12-21 (antibodies).

Support for claim 47, which recites, *inter alia*, that "the beads of each type are encoded with a chemical label that uniquely identifies the biomolecules attached to said bead type" is found at page 27, lines 21-23, which states "[t]he present method relies on the functional element of the invention to assemble a planar array of a multi-component mixture of beads which carry chemical labels in the form of tag molecules and may be so identified subsequent to performing the assay."

Support for claim 48, which recites, *inter alia*, that "the beads are on an electrode" is found at page 11, line 25 to page 12, line 19, which teaches a method of fabricating an electrochemical cell for the beads using a semiconductor (e.g., silicon or indium tin oxide) as an electrode.

Support for claim 49, which recites, *inter alia*, that "the beads are on a silicon chip" is found at page 7, line 25, which states that "[t]he integration of biochemical analytical techniques into a miniaturized system on the surface of a planar substrate {"chip") would yield substantial improvements...of analytical and diagnostic procedures". Additional support is found at page 11, line 25 to page 12, line 14, which teach a method of using silicon as a substrate for the beads.

Support for claim 50, which recites

> An array of biomolecules comprising a plurality of subarrays that are spatially separated from each other, wherein each of the subarrays is an array of claim 47, and wherein the location of the subarrays, in conjunction with the unique chemical label associated with each type of beads located in that subarray, uniquely identifies the biomolecules placed therein

is found at page 14, lines 4-6, which states "particles of distinct chemical type, introduced into the electrochemical cell at different times or injected in different locations, can be kept in spatially isolated locations by using this operation." Additional support for claim 50 is found at page 27, lines 21-23, which states "[t]he present method relies on the functional element of the invention to assemble a planar array of a multi-component mixture of beads which carry chemical labels in the form of tag molecules and may be so identified subsequent to performing the assay."

Support for claim 51, which recites "[t]he array claim 43, further comprising one or more analyte compounds, wherein said analyte compounds form analyte-biomolecule complexes with

the biomolecules attached to said beads," is found at page 27, lines 16-23, which states

> The present invention provides a method to produce a heterogeneous panel of beads and potentially of biomolecules for presentation to analytes in an adjacent liquid. A heterogeneous panel contains particles or biomolecules which differ in the nature of the chemical or biochemical binding sites they offer to analytes in solution. In the event of binding, the analyte is identified by the coordinates of the bead, or cluster of beads, scoring positive. The present method relies on the functional elements of the invention to assemble a planar array of a multi-component mixture of beads which carry chemical labels in the form of tag molecules and may be so identified subsequent to performing the assay.

Support for claims 52 and 53, which recite that "the formation of the analyte-biomolecule complexes results in an optical signature being associated with said complexes, and the detection of the complexes is accomplished by detecting the presence of the optical signature" (claim 52), and that "the optical signature comprises a fluorescent signal" (claim 53), is found at page 34, lines 9-13, which states

> The methods of the present invention readily facilitate competitive binding assays. For example, subsequent to binding of a fluorescent probe to a target-decorated bead in solution and the formation of a planar bead array adjacent to the electrode, fluorescent areas within the array indicate the position of positive targets, and these may be further probed by subjecting them to competitive binding.

Finally, support for claim 56, which recites that "the analyte compounds are selected from the group consisting of peptides, proteins, oligonucleotides, nucleic acids, ligands, receptors, antibodies, and antigens is found at page 29, lines 1-2 (ligands), page 33 lines 24-30 (receptors and antigens), page 43 lines 12-21 (antibodies), page 34, lines 9-17, and page 44, lines 4-8 (proteins and oligonucleotides), page 44, lines 11-24 (nucleic acids), and page 41, lines 9-13 (peptides).

Accordingly, Applicant respectfully submits that the effective filing date for claims 43-53

and 56 is April 25, 1996, the filing date of the provisional application. Therefore, Chandler (WO99/19515) and Walt (WO99/18434) are not prior art references under 35 U.S.C. §102(e) for purposes of determining the patentability of the pending claims.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. §102(e).

REJECTIONS UNDER 35 U.S.C. §103

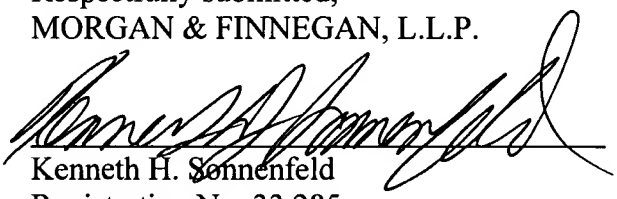
Claim 48 is rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Chandler or Walt in view of Koopal et al. (U.S. 5,422,246). Applicant respectfully traverses this rejection.

For reasons set forth above in connection with the Applicant's response to the §102 rejections, Chandler and Walt are not prior art references for purposes of determining the patentability of claim 48. Koopal et al. do not teach or suggest the claimed encoded bead array useful for performing binding assays.

In view of the amendments set forth herein and above remarks, Applicant respectfully maintains that the pending claims are allowable and solicit the issuance of a notice to such effect. If a telephone interview is deemed to be helpful to expedite the prosecution of the subject application, the Examiner is invited to contact Applicant's undersigned attorney at the telephone number provided.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: February 11, 2003

By: 
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